REMARKS

In the Office Action, dated January 18, 2008, the Examiner rejected claims 27 and 28 under 35 U.S.C. § 102 as being anticipated by U.S. Patent No. 4,702,829 to Polaschegg et al. ("Polaschegg"); rejected claims 29 and 30 under 35 U.S.C. § 103(a) as being unpatentable over Polaschegg in view of U.S. Patent No. 6,572,641 to Brugger et al. ("Brugger"); rejected claims 12 and 13 under U.S.C. § 103(a) as being unpatentable over Polaschegg in view of American Journal of Kidney Diseases, Vol. 38, No. 3 (September), 2001, pages 575-79 by Leypoldt et al. ("Leypoldt"); and rejected claims 14 and 15 under U.S.C. § 103(a) as being unpatentable over Polaschegg in view of Leypoldt and further in view of Brugger.

By this Reply, Applicant has amended claims 12-15 and 27-30. Claims 1-30 are currently pending in this application. No new matter has been added by this Reply.

REJECTION UNDER § 102(b)

In the Office Action, the Examiner rejected claims 27 and 28 under 35 U.S.C. § 102 as being anticipated by Polaschegg. Applicant traverses this rejection.

In order to properly anticipate Applicant's claims under § 102, a single prior art reference must disclose each and every element of the claim at issue, either expressly or under principles of inherency. Further, "[t]he identical invention must be shown in as complete detail as is contained in the. . . claim." *See* M.P.E.P. § 2131. Also, "[t]he elements must be arranged as required by the claim." Id.

Polaschegg discloses "a hemodiafiltration apparatus which comprises a conventional dialyzer 12 which is divided by a membrane 14 into a chamber traversed by the dialysis solution or rinsing liquid 16 and a chamber 18 traversed by the blood." (Col. 4, ll. 41-45.) Thus, Polaschegg discloses a conventional hemodiafiltration

apparatus. Polaschegg, however, does not disclose a "device configured to remove partially carrier bound substances from blood" (emphasis added), as recited in amended claim 27. It is known that conventional hemodialysis treatment removes small water soluble substances from the blood., while conventional hemodiafiltration treatment removes somewhat bigger water soluble substances from the blood. It is further known, however, that conventional hemdiafiltration treatment is not intended to remove larger substances, such as partially protein bound substances from the blood.

Polaschegg also discloses first and second sterile filters 44 and 78 that are used in the fluid circuit to clean the dialysis solution. (Col. 6, ll. 35-47.) No blood is pumped through these filters, thus filters 44 and 78 do not participate in the actual cleaning of the blood. The blood is instead pumped through the chamber 18 of the dialyzer 12. (Col. 5, ll. 56-58.) Sterile filters 44 and 78 work like an ultra filter for cleaning the replacement fluid before it is mixed with the blood (similar to dialyzer 40 of Applicant's disclosure).

Unlike the first and second filters 44 and 78 of Polaschegg, amended claim 27 recites a "filter having a semipermeable membrane separating a fluid compartment from a blood compartment, provided with means for mixing blood and a cleaning fluid and directing said mixture through the blood compartment, and . . . wherein the filter has a water permeability coefficient L_pA of at least 10 ml/min/mm Hg" (emphasis added). It should be noted that because there is blood on one side of the compartment of the claimed apparatus, the suction across the membrane takes place from the blood. As is known to those of ordinary skill in the art, there is a fundamental difference in dialyzer behavior between suction from water and suction from blood. For example, in the article "A New Semiempirical Mathematical Model for Prediction of Internal Filtration in

Hollow Fiber Hemodialyzers" (relevant portions of article are provided in the IDS filed concurrently with this Reply) it is stated that the water permeability coefficient is consistently lower, by about one third, when suction is from blood rather than water. (See page 566, 2nd column, 1st paragraph.) Please also see "Effect of Protein Adsorption on Diffusive and Convective Transport Through Polysulfone Membranes" and "*In Vitro* Evaluation of the Hydraulic Permeability of Polysulfone Dialyzers," which are also provided in the IDS filed concurrently with this Reply.

Because the filters of Polaschegg that discuss a water permeability coefficient only have dialysis solution passing through them, Polaschegg does not disclose a "filter having a semipermeable membrane separating a fluid compartment from a blood compartment, provided with means for mixing blood and a cleaning fluid and directing said mixture through the blood compartment, and . . . wherein the filter has a water permeability coefficient L_pA of at least 10 ml/min/mm Hg" (emphasis added).

Polaschegg also does not disclose a "filter [that] has a water permeability coefficient L_pA of at least 10 ml/min/mm Hg," as recited in amended claim 27 (emphasis added). Rather, Polaschegg discloses "a semipermeable membrane . . . which has a water permeability of about 30-600 ml/(m^2 h mmHg), in particular about 100-300 ml/(m^2 h mmHg). According to the invention it is advantageous for this first sterile filter to have a considerably higher water permeability than the second sterile filter. The ratio of the water permeability of the first sterile filter compared with the second sterile filter should lie in a range from 2:1 to 6:1, in particular at about 4:1." (Col. 3, ll. 33-41.)

In order to compare Polaschegg to claim 27, the units of Polaschegg must be converted. For example, the F60 dialyzer of Polaschegg has a water permeability of about 210 ml/(m^2h x mmHg) and a surface area of about 1.2 m^2. (Col. 3, ll. 46-50.) The

conversion of units is as follows: 210 x 1.2 m^2 = 252 ml/h/mmHg = 252/60 ml/min/mmHg = 4.2 ml/min/mmHg, which is the water permeability coefficient when suction occurs from water. As described above, in order to determine the water permeability coefficient when suction occurs from blood, this number must be divided by a factor of approximately 3. Even if one assumes the maximum case of Polaschegg where the surface area is 1.5 m^2 and the water permeability is 600 ml(m^2h mmHg) (see col. 3, ll. 33-45.), the result is 600 x 1.5/60 = 15 ml/min/mmHg, which must be divided by approximately a factor of 3 to obtain a water permeability value when suction occurs from blood. Thus, Polaschegg does not disclose a "filter that [has] a water permeability coefficient L_pA of at least 10 ml/min/mm Hg," as recited in amended claim 27 (emphasis added).

For at least the aforementioned reasons, amended independent claim 27 is allowable over the cited reference, and thus, the § 102(b) rejection of independent claim 27 should be withdrawn. Further, claim 28 is allowable over the cited reference at least due to its dependence from allowable independent claim 27. Accordingly, the rejection of claim 28 should also be withdrawn.

REJECTIONS UNDER § 103(a)

In the Office Action, the Examiner rejected claims 29 and 30 under 35 U.S.C. § 103(a) as being unpatentable over Polaschegg in view of Brugger.

Brugger discloses "[a]n external fluid warming device . . . that includes a fluid warming chamber and an air separation chamber. The fluid warming chamber has a fluid inlet that communicates with a fluid pathway. . . The fluid inlet is connected to a source of fluid and the fluid outlet is connected to an output device, such as an ultrafiltration machine." (Abstract.)

Brugger, however, does not disclose a "filter [that] has a water permeability coefficient L_pA of at least 10 ml/min/mm Hg," as recited in amended independent claim 27. Thus, Brugger does not cure the deficiencies of Polaschegg discussed above. Because claims 29 and 30 ultimately depend from independent claim 27, dependent claims 29 and 30 are allowable over the cited references and the § 103(a) rejection of claims 29 and 30 should be withdrawn.

In the Office Action, the Examiner also rejected claims 12 and 13 under U.S.C. § 103(a) as being unpatentable over Polaschegg in view of Leypoldt. Applicant respectfully traverses this rejection.

Several basic factual inquires must be made in order to determine the obviousness or non-obviousness of claims of a patent application under 35 U.S.C. § 103. These factual inquiries, set forth in Graham v. John Deere Co., 383 U.S. 1, 17, 148 U.S.P.Q. 459, 467 (1966), require the Examiner to:

(1) Determine the scope and content of the prior art;

(2) Ascertain the differences between the prior art and the claims in issue;

(3) Resolve the level of ordinary skill in the pertinent art; and

(4) Evaluate evidence of secondary considerations.

The obviousness or non-obviousness of the claimed invention is then evaluated in view of the results of these inquiries. Graham, 383 U.S. at 17-18, 148 U.S.P.Q. at 467; see also KSR Internat'l Co. v. Teleflex Inc., 82 U.S.P.Q.2d 1385 (U.S. 2007); see also M.P.E.P. § 2141(II).

Polaschegg discloses "a hemodiafiltration apparatus which comprises a conventional dialyzer 12 which is divided by a membrane 14 into a chamber traversed

by the dialysis solution or rinsing liquid 16 and a chamber 18 traversed by the blood." (Col. 4, ll. 41-45.) Leypoldt discloses a hemodialysis system (see page 575).

As discussed above, however, Polaschegg does not disclose or suggest "a water permeability coefficient L_pA of the filter is at least 10 ml/min/mm Hg," as recited in amended independent claim 12. For the purposes of this rejection, the Examiner has relied on Polaschegg to meet this limitation of amended independent claim 12. The Examiner does not contend that Leypoldt discloses or suggests a filter having a "water permeability coefficient L_pA" of "at least 10 ml/min/mm Hg." In fact, Leypoldt fails to cure this deficiency of Polaschegg. Accordingly, for at least this reason, amended claim 12 is allowable over the cited references. Thus, dependent claim 13 is allowable due at least to its dependence from allowable independent claim 12.

Moreover, neither Polaschegg nor Leypoldt, discloses a "method for removing partially carrier bound substances from blood." As noted above, it was known in the art at the time of the invention that hemodialysis treatments, as disclosed in Leypoldt, are only intended to remove small water soluble substances from the blood.

The Examiner further alleges that "Leypoldt et al teach that the urea and creatinine mass transfer area coefficients were independent of blood flow rate but increased when dialysate i.e. cleaning fluid was increased from 500 to 800 ml/min in high flux dialyzers (see abstract in page 575). Hence any dialysate flow greater than 1000 ml/min would further enhance mass transfer area coefficients of small solutes and the increased ratio between the dialysate flow rate and the blood flow rate would also enhance mass transfer area coefficients of small solutes for increased removal of small solutes through the membrane in high flux dialyzers. It would have been obvious to one having ordinary skill in the art at the time the invention was made to optimize the

dialysate flow rate as well as the ratio between the dialysate flow rate and the blood flow rate in the method of Polaschegg et al to arrive at optimal removal of small solutes by enhancing mass transfer coefficients of small solutes as suggested by Leypoldt et al." (Office Action at 4.) Applicant disagrees.

Leypoldt does not teach or suggest "a water permeability coefficient L_pA of the filter is at least 10 ml/min/mm Hg; the cleaning fluid flow rate is at least 1000 ml/min; and a ratio between the cleaning fluid flow rate and a blood flow rate is at least 5." It appears that the Examiner has confused clearance, which is the cleaning capacity of the dialyzer at the existing flow rate (blood and dialysis fluid), with k_0A. In theory k_0A is a dialyzer constant that can be used together with the flow rates to calculate clearance. It is measured in ml/min, and is theoretically the clearance obtained at infinite flow rates (blood and dialysis fluid).

Leypoldt has shown that k_0A is not constant for dialysis flows of 500 to 800 ml/min. (Page 576.) Leypoldt states that this might be due to a bad distribution of the liquid in the dialyzer, an effect which becomes less dominant with higher flows. (Page 578.) The k_0A increases with an increase of the flow up to a certain lever, where k_0A stagnates.

For large dialyzers, as usually used in dialysis treatments, and used in the work of Leypoldt, clearance is numerically often close to the blood flow rate. Increasing the k_0A of the dialyzer then has a small influence on the clearance. This also means that backwards calculation of k_0A from measured clearances and flow rates will result in large increases in calculated k_0A even for small increases in clearance.

Accordingly, Applicant does not agree with the Examiner's interpretation that clearance will continually increase with increased flow. As noted above, clearance is

not equivalent to k_0A except for the case of an infinite blood flow and dialysis fluid flow. However, even if clearance were equivalent to k_0A, the increase in k_0A with increased flow only goes up to a certain level, where k_0A stagnates. And even if k_0A increases, the clearance will not increase to any significant extent if the blood flow does not increase. Clearance can never be larger than the blood flow in Leypoldt.

For removal of partially protein bound substances according to the claimed invention, the blood flow is not a limiting factor. In fact, in order to increase the removal of partially protein bound substances, the dialyzer size and the flow rate of the dialysis fluid should be increased simultaneously. The limiting factor of Leypoldt is the blood flow, and thus, an increased blood flow rate is the only way that Leypoldt could achieve better clearance.

For at least these additional reasons, Applicant submits that neither Polaschegg nor Leypoldt teach or suggest "a water permeability coefficient L_pA of the filter is at least 10 ml/min/mm Hg; the cleaning fluid flow rate is at least 1000 ml/min; and a ratio between the cleaning fluid flow rate and a blood flow rate is at least 5," as recited in amended independent claim 12. Thus, amended independent claim 12 is allowable over the prior art and the Examiner should withdraw this rejection. Also, because claim 13 properly depends from claim 12, the Examiner should withdraw the rejection of claim 13.

The Examiner also rejected claims 14 and 15 under U.S.C. § 103(a) as being unpatentable over Polaschegg in view of Leypoldt and further in view of Brugger. Applicant respectfully traverses this rejection.

As noted above, Brugger discloses "[a]n external fluid warming device . . . that includes a fluid warming chamber and an air separation chamber. The fluid warming

chamber has a fluid inlet that communicates with a fluid pathway. . . The fluid inlet is connected to a source of fluid and the fluid outlet is connected to an output device, such as an ultrafiltration machine." (Abstract.)

Brugger, however, does not disclose or suggest that "a water permeability coefficient L_pA of the filter is at least 10 ml/min/mm Hg; the cleaning fluid flow rate is at least 1000 ml/min; and a ratio between the cleaning fluid flow rate and a blood flow rate is at least 5" as recited in claim 12. Thus, Brugger does not cure the deficiencies of Polaschegg and Leypoldt discussed above. Because dependent claims 14 and 15 ultimately depend from allowable independent claim 12, dependent claims 14 and 15 are allowable over the cited references and the § 103(a) rejection of claims 14 and 15 should be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, Applicant respectfully requests reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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